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Understanding Barriers and Facilitators of Pre-exposure Prophylaxis (PrEP) Among Transgender and Gender Diverse Adults in an Integrated Health Care System

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Abstract
Transgender and gender diverse individuals face health disparities such as higher HIV prevalence, but limited studies have found low PrEP uptake among these populations. To understand both patient and provider perspectives regarding PrEP care for transgender and gender diverse individuals, we conducted a mixed-methods study at Kaiser Permanente Southern California from September 2020 to October 2021. Transgender and gender diverse adults (N = 396) participated in a web-based survey, and qualitative interviews were subsequently conducted with a subset of survey respondents (N = 32) and healthcare providers (N = 8). Among survey respondents, > 75% were familiar with PrEP, and > 40% reported at least one HIV risk factor, but < 5% had taken PrEP. Interview themes included increasing providers' inclusivity in primary care for transgender and gender diverse patients, and reducing logistical barriers and costs associated with PrEP-related visits. To improve PrEP uptake among transgender and gender diverse individuals, barriers across patient, provider, and health system levels must be addressed.

Keywords Transgender · Gender diverse · PrEP · HIV · Prevention

Introduction

Approximately 1.2 million individuals in the United States (U.S.) are living with HIV, with an estimated 34,800 new HIV infections occurring in 2019 [1, 2]. Rates of new HIV infections are highest among persons aged 25–34, followed by persons aged 35–44 years, and among Black/African American persons, followed by Hispanic/Latino persons and multiracial persons [2]. Transgender individuals, particularly transgender women, face health disparities, including higher prevalence of HIV [3–6]. Data have shown that transgender women in the U.S. are 34 times more likely to be living with HIV than the general population [7]. Gender diverse (e.g., non-binary) individuals are also at increased risk of HIV, although data are extremely limited [8].

Pre-exposure prophylaxis (PrEP) for HIV prevention is highly efficacious when taken as prescribed [9]. However, evidence of PrEP efficacy among transgender and gender diverse individuals is lacking, likely due to underrepresentation of these groups in clinical trials and suboptimal adherence [10, 11]. Studies of the PrEP care cascade among transgender and gender diverse individuals in both health system and community settings have identified major gaps in linkage to PrEP care and persistence on PrEP [12, 13].

Identifying and addressing barriers to PrEP among those at risk for HIV can contribute to greater PrEP access and uptake. Transgender and gender diverse individuals may face unique barriers to PrEP and require different implementation strategies than men who have sex with men [14]. Findings from focus groups with transgender women in a study in New York found that participants were often skeptical of the benefits of PrEP and were concerned the messaging around

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PrEP oversimplified risks and benefits [15]. Studies in other U.S. cities have shown that mistrust of the health care system, lack of PrEP knowledge, stigma, concerns about side-effects, and need for improved provider communication can impact PrEP uptake [16–20]. Moreover, barriers are exacerbated for Black transgender women, who have lower awareness of PrEP and willingness to use PrEP compared with those of other race/ethnicity groups [13, 21].

Few studies have assessed perspectives of both transgender and gender diverse individuals and their health care providers regarding PrEP. Understanding patient, provider, and health system-level barriers to PrEP use and identifying opportunities to improve care for transgender and gender diverse individuals within the health system context is critical to inform multipronged strategies to improve PrEP uptake and care retention. In this mixed-methods study among transgender, gender diverse individuals, and primary care providers in a large integrated health system in California, we sought to examine PrEP knowledge and experience, HIV risk, barriers to PrEP use, and suggestions for improving PrEP care.

Methods

Study Setting and Overview

Kaiser Permanente Southern California (KPSC) is a large integrated health care delivery system serving over 4.7 million members with diverse racial/ethnic backgrounds generally similar to the underlying Southern California population [22]. KPSC members are enrolled through employer-provided, pre-paid, or federally sponsored insurance plans. Comprehensive electronic health records (EHR) collect all details of care received, including diagnoses, laboratory tests, procedures, and pharmacy data.

KPSC offers comprehensive transgender care, including gender-affirming surgeries (at a centralized location), hormone therapy, gynecologic services, fertility preservation, and other services available across the Southern California region. PrEP is mainly managed by referral to designated PrEP care coordinators in the infectious disease department. Some PrEP patients go to their primary care provider (PCP) for routine PrEP care, but new patients are usually referred to the infectious disease department for initial consultation and baseline lab tests. PrEP is a covered benefit (with a medication and service co-pay depending on drug benefit and insurance coverage level).

The study, conducted between September 2020 and October 2021, comprised a survey of transgender and gender diverse adults, as well as in-depth telephone interviews with a subset of survey respondents. In-depth interviews were also conducted with PCPs, including those with transgender and gender diverse patients on their panel. The study was approved by the KPSC Institutional Review Board (IRB), which waived the requirement for written informed consent due to minimal risk to study participants.

Survey Participants and Procedures

We identified potential survey participants through a KPSC EHR transgender registry, which includes near real-time data on individuals who received diagnosis codes for gender identity disorder or gender dysphoria, or who received hormones and/or surgical procedures for gender reassignment. We included individuals with active KPSC health plan membership and age between 18 and 70 years. To avoid sending the survey to individuals who may have been at end stages of life or who would no longer benefit from PrEP, we excluded those with a diagnosis of HIV, metastatic cancers, or end stage renal diseases, or those who were living in a skilled nursing facility or receiving palliative care.

A secure link for the web-based survey was sent to eligible individuals via email through REDCap©, a secure web application for managing online surveys. The initial email invitation included an information sheet with "consent form-like" language, which outlined the purpose of the study, their participation rights, and contact information for the IRB and study team. The survey was provided in English or Spanish, depending on individuals' preferred language, and was open from September through December 2020. We attempted to contact eligible individuals four times including the initial invitation email and three reminder emails. If we did not receive a response after the fourth email, these individuals were considered non-responders. For those who did not provide a valid email address on their EHR (approximately 7%), a paper survey was mailed with a return envelope and prepaid postage. No monetary incentives were offered to participate in the survey.

Survey Content

The survey questions were informed by the Andersen behavioral model of health care utilization [23]. We chose this model to guide our survey questions, as it addresses predisposing factors, need factors, and enabling factors that determine why or why not transgender and gender diverse persons may seek PrEP within an integrated health care system such as KPSC. We collected information regarding predisposing factors such as self-reported sociodemographic characteristics, gender identity, sexual orientation, marital status, and comorbid conditions in the prior 6 months (chronic pain, anxiety, depression, post-traumatic stress disorder, bipolar, HIV/AIDS, hepatitis B, and hepatitis C). We asked about need factors including recent sexual behaviors, history of bacterial sexually transmitted infections (STIs)

including gonorrhea, chlamydia, and/or syphilis, and non-prescription injectable and non-injectable recreational drug use in the prior 6 months. We also asked about enabling factors, such as awareness of PrEP, knowledge of names of currently available medications approved for PrEP, and correct statements regarding PrEP use. In addition, we asked about current PrEP use or PrEP use for ≥ 1 month in the prior 6 months, as well as perceived barriers to PrEP use.

Transgender Participant Interviews

Qualitative interviews were conducted among a subset of survey respondents (N = 32) who had indicated in their survey response that they were interested in participating in an interview. Individuals were purposively selected to include variation by age, race/ethnicity, and gender within each of four groups: current and previous PrEP users, individuals reporting HIV risk factors but not using PrEP, and individuals not reporting HIV risk factors and not using PrEP. The interviews were conducted by trained research staff using interview guides with open-ended questions that probed about the following domains: (1) experience with PrEP (knowledge or use), (2) barriers and challenges with using PrEP, (3) experience with providers, (4) referral process for PrEP initiation, and (5) suggestions for improving PrEP care. The phone interview took approximately 30 min, and a $50 gift card was offered to the participants upon completion.

Provider Interviews

We also conducted interviews among gender health services and transgender care physician leads and PCPs. Providers were asked about: (1) current practices of PrEP eligibility assessment and PrEP referral, (2) barriers to discussing HIV risk, PrEP use, and PrEP referral, and (3) providers' needs for training or organizational support for integrating PrEP eligibility assessment and referral into workflows. The semi-structured telephone interviews took approximately 30 min to complete, and no renumeration was offered per standard regulations.

Data Analysis

To analyze the survey data, we described and compared the distribution of self-reported characteristics among transgender women, transgender men, or gender diverse individuals [agender, genderqueer, gender non-conforming, gender fluid, gender non-binary, anti-gender, bigender, intersex, partial androgen insensitivity syndrome (PAIS)], using the χ^2 test for categorical variables. We described the proportions in each group reporting PrEP awareness, knowledge, and use, and we compared the frequency of self-reported behaviors and barriers to PrEP use by group. Analyses were performed using the SAS Enterprise Guide (version 7.1; SAS Institute).

All telephone interviews were audio-recorded using Microsoft TEAMS and transcribed by a professional transcription service. Thematic analysis was conducted using NVivo12 Plus (QSR International). We used a deductive approach to develop codes based on the key domains in patient and provider interview scripts and an inductive approach to develop codes emanating from the data. Two team members trained in qualitative analysis [CP and MM] coded a random sample of transcripts (N = 10) and met to review and compare coding results and annotations; discrepancies were then resolved. MM then coded the remaining transcripts. At the completion of the coding process, CP and MM developed summary reports with quotes highlighting the themes and sub-themes that emerged from each of the domains supporting our research questions.

Results

Survey Results

The survey was sent to 4398 individuals, with 436 completing the survey (response rate of approximately 10%). Compared to non-responders, survey respondents were older [mean (standard deviation) age in years 34.2 (13.53) vs. 30.8 (11.98) years], more were of White race (59.2% vs. 40.9%), and more had commercial insurance without a high deductible (58.5% vs. 53.7%). We excluded 40 survey respondents who did not self-identify as transgender or gender diverse, or who self-reported as HIV-positive. Overall, 396 survey respondents were included in the analysis, including 167 transgender men, 151 transgender women, and 78 gender diverse individuals.

More than half of all survey respondents were aged 18–32 years, but compared with transgender men or gender diverse individuals, transgender women were older (Table 1). Most respondents identified as White (62.6%) or Hispanic/Latino (29.3%). Approximately 60% of respondents had commercial insurance without a high deductible, and fewer transgender women had Medicaid compared to transgender men and gender diverse individuals; however, almost all respondents (> 98%) reported a prescription drug benefit (usually with fixed co-pays). More transgender men identified as heterosexual, whereas more transgender women identified as bisexual.

HIV risk factors were common among survey respondents, with at least one HIV risk factor reported by 41.9% of transgender men, 39.1% of transgender women, and 52.6% of gender diverse individuals (Fig. 1), although only a small proportion of individuals reported that they thought they might be at risk of HIV infection (4.8% of transgender men,

Table 1 Demographic characteristics of transgender and gender diverse survey respondents

Characteristic	Transgender men[†] n (%)	Transgender women[†] n (%)	Gender diverse[‡] n (%)	Total n (%)	p value*
N	167	151	78	396	
Age					< 0.0001
18–32	116 (69.5)	61 (40.4)	54 (69.2)	231 (58.3)	
33–45	33 (19.8)	38 (25.2)	17 (21.8)	88 (22.2)	
46–58	10 (6.0)	34 (22.5)	3 (3.8)	47 (11.9)	
59+	8 (4.8)	18 (11.9)	4 (5.1)	30 (7.6)	
Insurance					0.0378
Commercial, without high deductible	103 (61.7)	90 (59.6)	39 (50)	232 (58.6)	
Medicare	2 (1.2)	11 (7.3)	6 (7.7)	19 (4.8)	
Medicaid	18 (10.8)	8 (5.3)	13 (16.7)	39 (9.8)	
High deductible	33 (19.8)	30 (19.9)	11 (14.1)	74 (18.7)	
Private pay	8 (4.8)	8 (5.3)	7 (9.0)	23 (5.8)	
Other/missing	3 (1.8)	4 (2.6)	2 (2.6)	9 (2.3)	
Race[§]					0.2208
White	103 (61.7)	97 (64.2)	48 (61.5)	248 (62.6)	
Asian	9 (5.4)	14 (9.3)	2 (2.6)	25 (6.3)	
Black	8 (4.8)	1 (0.7)	3 (3.8)	12 (3.0)	
Other/multiple	45 (26.9)	38 (25.2)	23 (29.5)	106 (26.8)	
Missing	2 (1.2)	1 (0.7)	2 (2.6)	5 (1.3)	
Hispanic/Latino	53 (31.7)	38 (25.2)	25 (32.1)	116 (29.3)	0.1722
Sexual orientation					< 0.0001
Heterosexual or straight	56 (33.5)	30 (19.9)	1 (1.3)	87 (22.0)	
Gay	24 (14.4)	5 (3.3)	9 (11.5)	38 (9.6)	
Lesbian	2 (1.2)	29 (19.2)	8 (10.3)	39 (9.8)	
Bisexual	53 (31.7)	58 (38.4)	21 (26.9)	132 (33.3)	
Other	29 (17.4)	23 (15.2)	38 (48.7)	90 (22.7)	
Prefer not to answer	3 (1.8)	6 (4.0)	1 (1.3)	10 (2.5)	
Education					0.2094
Less than high school	1 (0.6)	5 (3.3)	2 (2.6)	8 (2.0)	
12th grade (high school graduate or GED)	20 (12.0)	15 (9.9)	7 (9.0)	42 (10.6)	
Some college or technical school	83 (49.7)	60 (39.7)	27 (34.6)	170 (42.9)	
Bachelor's degree	43 (25.7)	41 (27.2)	26 (33.3)	110 (27.8)	
Graduate degree	20 (12.0)	29 (19.2)	16 (20.5)	65 (16.4)	
Prefer not to answer	0 (0)	1 (0.7)	0 (0)	1 (0.3)	
Income					
≤ $35,000	44 (26.3)	31 (20.5)	23 (29.5)	98 (24.7)	0.4588
$35,001–$65,000	38 (22.8)	38 (25.2)	17 (21.8)	93 (23.5)	
$65,001–$100,000	33 (19.8)	30 (19.9)	18 (23.1)	81 (20.5)	
> $100,001	26 (15.6)	37 (24.5)	10 (12.8)	73 (18.4)	
Prefer not to answer	6 (3.6)	4 (2.6)	2 (2.6)	12 (3.0)	
I do not know	20 (12.0)	11 (7.3)	8 (10.3)	39 (9.8)	
Marital status					0.4038
Married	25 (15.0)	33 (21.9)	8 (10.3)	66 (16.7)	
Not married but in a committed relationship	42 (25.1)	30 (19.9)	20 (25.6)	92 (23.2)	
Widowed	0 (0)	1 (0.7)	0 (0)	1 (0.3)	
Single, divorced, or separated	96 (57.5)	85 (56.3)	48 (61.5)	229 (57.8)	
Prefer not to answer	4 (2.4)	2 (1.3)	2 (2.6)	8 (2.0)	
Self-reported comorbidities[¶]					
At least one comorbidity reported	76 (45.5)	51 (33.8)	36 (46.2)	163 (41.2)	0.0637

Table 1 (continued)

Characteristic	Transgender men† n (%)	Transgender women† n (%)	Gender diverse‡ n (%)	Total n (%)	p value*
More than one comorbidity reported	54 (32.3)	37 (24.5)	29 (37.2)	120 (30.3)	0.1066
Chronic pain	16 (9.6)	10 (6.6)	13 (16.7)	39 (9.8)	0.0532
Anxiety	64 (38.3)	40 (26.5)	31 (39.7)	135 (34.1)	0.0424
Depression	60 (35.9)	40 (26.5)	24 (30.8)	124 (31.3)	0.1923
Post-traumatic stress disorder	16 (9.6)	9 (6)	11 (14.1)	36 (9.1)	0.1219
Bipolar	9 (5.4)	3 (2)	5 (6.4)	17 (4.3)	0.1926
HIV/AIDS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Hepatitis B	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Hepatitis C	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
None	91 (54.5)	100 (66.2)	42 (53.8)	233 (58.8)	0.0637

*Chi-square p-value

†Individuals who identified as transgender man, transgender woman, different gender than their reported sex at birth, or based on other self-reported survey responses identifying themselves as transgender man or transgender woman

‡Gender diverse includes agender, genderqueer, gender non-conforming, gender fluid, non-binary, anti-gender, bigender, intersexed, and PAIS

§Self-reported race with American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and biracial included in Other/Missing

¶Reported being diagnosed in the past 6 months

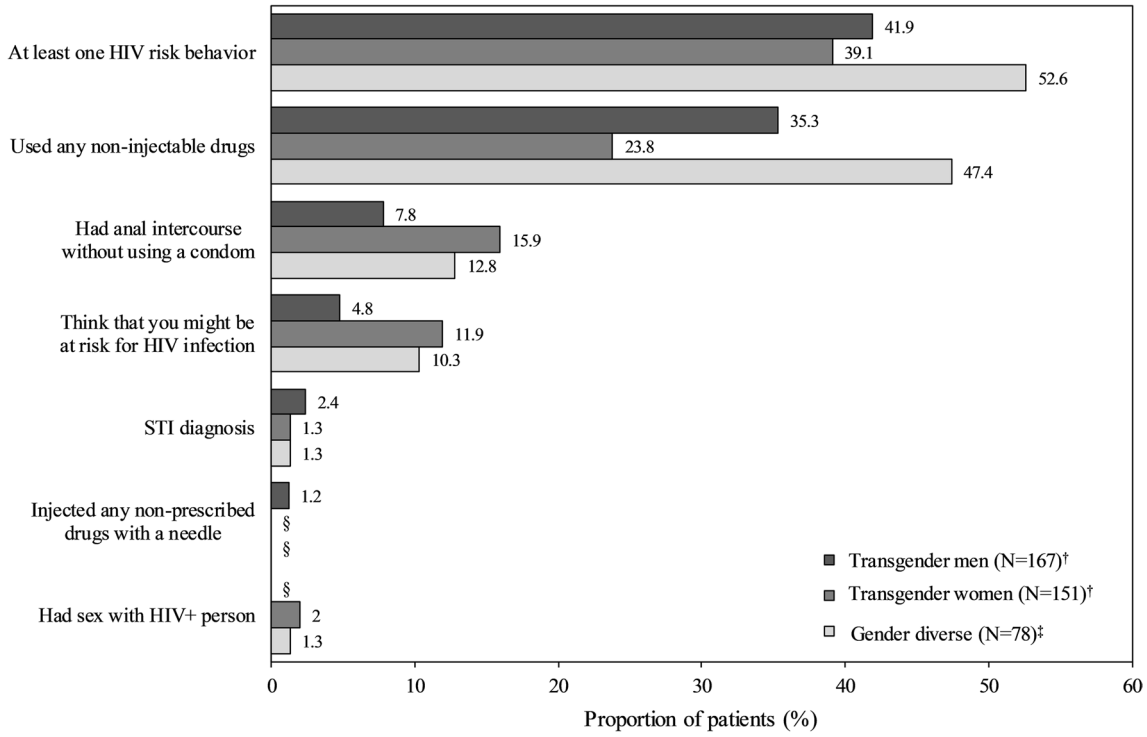

Fig. 1 Self-reported risk factors for HIV acquisition in the prior 6 months among transgender and gender diverse survey respondents. †Individuals who identified as transgender man, transgender woman, different gender than their reported sex at birth, or based on other self-reported survey responses identifying themselves as transgender man or transgender woman. ‡Gender diverse includes agender, genderqueer, gender non-conforming, gender fluid, non-binary, anti-gender, bigender, intersexed, and PAIS. §No respondents reported this statement

11.9% of transgender women, and 10.3% of gender diverse individuals). The most common risk factor reported among these groups was using non-injectable drugs (35.3%, 23.8%, and 47.4%, respectively), followed by having anal intercourse without using a condom (7.8%, 15.9%, and 12.8%, respectively).

Approximately 75% of all survey respondents were aware of PrEP as a medication for HIV prevention, but fewer could correctly identify brand names of PrEP (38.3% of transgender men, 37.7% of transgender women, and 50.0% of gender diverse individuals) (Table 2). More than 75% of survey respondents thought that people taking PrEP should continue to use condoms during sex. Although few respondents thought that taking PrEP increased the risk of other STIs, 41.3% of transgender men, 41.1% of transgender women, and 30.8% of gender diverse individuals were not sure if PrEP prevents other STIs. Only 4.2% of transgender men, 5.3% of transgender women, and 2.6% of gender diverse individuals in our study sample had taken PrEP for at least a month in the prior 6 months.

Among barriers to PrEP (Fig. 2), the most common barrier respondents reported was cost/affordability (67.7% of transgender men, 49.7% of transgender women, and 71.8% of gender diverse individuals), even though nearly all respondents had a prescription drug benefit. Other frequently reported barriers included possible side effects (43.1% of transgender men, 27.8% of transgender women, and 41.0% of gender diverse individuals), not having enough information about how PrEP works (44.3%, 28.5%, and 41.0%, respectively), and not being sure if PrEP was needed (40.7%, 31.8%, 41.0%, respectively).

Transgender Participant Interview Results

Of the 32 survey respondents recruited for in-depth interviews, 14 individuals were transgender women and 18 were transgender men. Of these, 7 individuals were current PrEP users, 3 were previous PrEP users, 14 had reported HIV risk factors in the survey but were not using PrEP, and 8 had not reported HIV risk factors and were

Table 2 Awareness, knowledge, and use of PrEP among transgender and gender diverse survey respondents

	Transgender men[†] n (%)	Transgender women[†] n (%)	Gender diverse[‡] n (%)	p value*
N	167	151	78	
Awareness of PrEP as medication for HIV prevention	122 (73.1)	109 (72.2)	65 (83.3)	0.1477
Recognized name of PrEP medications (Truvada, Descovy)	64 (38.3)	57 (37.7)	39 (50)	0.1553
Knowledge of PrEP use				
People using PrEP do not need to use condoms during sex	2 (1.2)	1 (0.7)	1 (1.3)	0.8611
People using PrEP should continue using condoms during sex	132 (79.0)	112 (74.2)	63 (80.8)	0.4348
People should not take PrEP when they drink alcohol	35 (21.0)	18 (11.9)	8 (10.3)	0.0310
People should not take PrEP if they are taking other medications	9 (5.4)	10 (6.6)	6 (7.7)	0.7725
I don't agree with any of the statements above	3 (1.8)	3 (2.0)	4 (5.1)	0.2612
I don't know/I am not sure	27 (16.2)	36 (23.8)	10 (12.8)	0.0765
Knowledge of PrEP and STIs				
Using PrEP helps prevent other sexually transmitted infections, including chlamydia, gonorrhea, and syphilis	10 (6.0)	11 (7.3)	0 (0)	0.0577
Using PrEP does not help prevent other sexually transmitted infections	84 (50.3)	72 (47.7)	50 (64.1)	0.0524
Using PrEP increases the risk for acquiring other sexually transmitted infections	3 (1.8)	6 (4.0)	2 (2.6)	0.4946
I don't agree with any of the statements above	3 (1.8)	5 (3.3)	3 (3.8)	0.5815
I don't know/I am not sure	69 (41.3)	62 (41.1)	24 (30.8)	0.2393
PrEP use				
Taking PrEP	4 (2.4)	7 (4.6)[§]	2 (2.6)	0.4937
PrEP use for at least 1 month within the last 6 months	7 (4.2)	8 (5.3)	2 (2.6)	0.6241

*Chi-square p-value

[†]Individuals who identified as transgender man, transgender woman, different gender than their reported sex at birth, or based on other self-reported survey responses identifying themselves as transgender man or transgender woman

[‡]Gender diverse includes agender, genderqueer, gender non-conforming, gender fluid, non-binary, anti-gender, bigender, intersexed, and PAIS

[§]One transgender woman who reported to taking PrEP at the time of the survey also reported not using PrEP for at least 1 month within the past 6 months

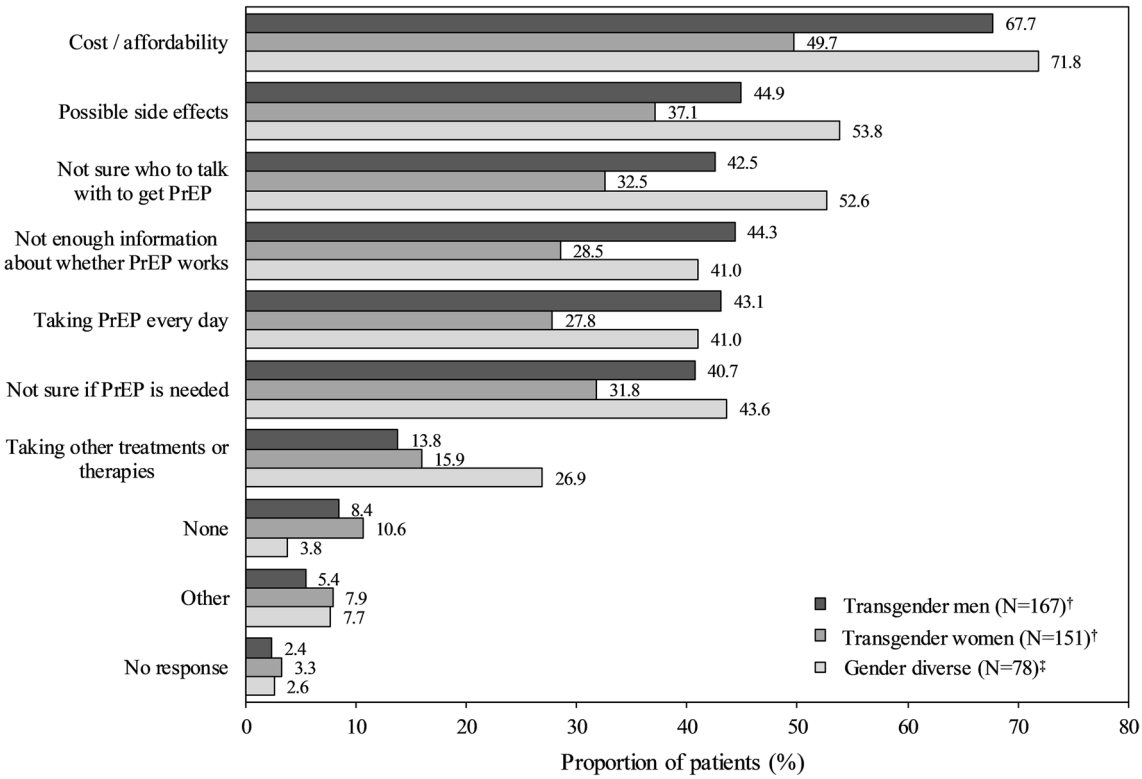

Fig. 2 Barriers to PrEP use among transgender and gender diverse survey respondents. †Individuals who identified as transgender man, transgender woman, different gender than their reported sex at birth, or based on other self-reported survey responses identifying themselves as transgender man or transgender woman. ‡Gender diverse includes agender, genderqueer, gender non-conforming, gender fluid, non-binary, anti-gender, bigender, intersexed, and PAIS

Table 3 Demographic characteristics of transgender interview participants

Characteristic	Current PrEP user n (%)	Previous PrEP user n (%)	At risk, not using PrEP n (%)	Not at risk, not using PrEP n (%)	Total n (%)
N	7	3	14	8	32
Age (years)					
Mean (SD)	36.3 (9.95)	24.3 (5.03)	31.8 (11.18)	33.4 (15.08)	32.5 (11.60)
Race/ethnicity					
Non-Hispanic White	3 (42.9)	2 (66.7)	6 (42.9)	2 (25.0)	13 (40.6)
Hispanic	1 (14.3)	0 (0.0)	5 (35.7)	2 (25.0)	8 (25.0)
Non-Hispanic Black	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	1 (3.1)
Non-Hispanic Asian	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (6.3)
Other/Multiple	1 (14.3)	1 (33.3)	2 (14.3)	4 (50.0)	8 (25.0)
Gender					
Transgender woman	4 (57.1)	1 (33.3)	7 (50.0)	2 (25.0)	14 (43.8)
Transgender man	3 (42.9)	2 (66.7)	7 (50.0)	6 (75.0)	18 (56.3)

not using PrEP (Table 3). Individuals had a range of prior experiences and knowledge of PrEP, with some having very little familiarity with PrEP and others having had positive experiences using PrEP and making it a part of their daily routine. However, clear themes emerged from the data across participant groups around barriers to PrEP uptake (Supplementary Table).

Need for Trans-inclusive Providers

All participants emphasized the importance of having providers that could relate well to transgender and gender diverse individuals. Although some participants were happy with their PCPs, other participants reported challenges such as being misgendered (e.g., provider used a pronoun different than patients' preferred pronouns) or being asked irrelevant questions (e.g., a transwoman being asked about her last Pap smear). Participants described not being asked questions about their sexual history, having to be proactive in talking with their doctors about PrEP, or switching doctors to find one they would be comfortable with. Several participants said that their PCPs were not knowledgeable about PrEP but referred them to infectious disease specialists.

When asked about discussing PrEP with their provider, a 39-year-old transgender man said, "PrEP didn't even come up [in encounter with physician], so I think for trans people especially, I don't think providers understand who it's for outside of gay men." A 54-year-old transgender woman expressed frustration regarding providers' limited knowledge of which communities PrEP might benefit. "It's still kind of a small community of physicians, who have knowledge about the transgender community," she shared. "I feel like there's far greater knowledge about the gay community versus the trans community."

A third interviewee echoed these concerns as a 21-year-old transgender man seeking PrEP information or a prescription from a provider. "Because I know a lot of my friends have this fear of going to the doctor's office and having to, first, explain to their doctor that they're trans, and then, how that affects everything else, and sort of feeling like they're going to the doctor's office with more knowledge than the professional."

Interest in More Relevant Information About PrEP

Most participants had learned about PrEP outside of the health care setting, such as through media or from their friends. Some had heard about PrEP but could not provide details as to how it relates to HIV prevention. A common theme was a lack of clarity about who can benefit from PrEP, with some participants wanting more information about what PrEP was for, and others saying they wanted more information on how PrEP worked for them, as a transgender woman, transgender man, or gender diverse individual.

One interviewee, a 56-year-old transgender man stated, "I'd never even heard of it. And, being in the community that I'm in … I've never even heard my gay friends, or anybody talk about it. So, there's probably a lack of information to them getting it." Another interviewee shared that they became familiar with PrEP primarily through social interactions and LGBTQ+ events as opposed to receiving information from a provider. The 43-year-old transgender man said, "I learned about it through my friends and my clients."

When asked who they felt might benefit from PrEP, a 20-year-old transgender man remarked, "I think that when I first learned about what PrEP was that it was only for people who were gay, cisgender, and engaging in sexual activities…" A separate young transgender man expressed concern regarding lack of research concerning transgender persons using PrEP. He told the study team, "I would feel a lot better if there were some sort of research about PrEP and trans individuals … I don't know if PrEP would be as effective, if I'm taking that as a trans person."

Excessive Cost and Time Required

Another pervasive theme in the data was concern about costs of PrEP and the time required to get PrEP prescriptions. Some respondents did not understand how they could get the costs of PrEP covered, and for some of those who were getting 100% coverage for PrEP, the cost of routine visits and laboratory tests was prohibitive. Others reported that the investment of time required to get laboratory tests done between PrEP prescriptions was challenging for them and had interrupted their PrEP care. They had to take time off work and other activities to attend appointments and get testing done. Some participants already had a lot of routine visits for other reasons, such that being referred to another specialist for a PrEP evaluation seemed burdensome.

Regarding these concerns, a 38-year-old transgender man shared, "I think the biggest barrier…is financial assistance because the lab work is very expensive." A second interviewee expressed hesitancy due to the burden of time requirements associated with obtaining or having a PrEP prescription. The 24-year-old transgender woman added, "I'm really busy sometimes and I don't have time to do… a blood test that needs to be done every 3 months for it, just to check up, make sure everything is okay … if I don't do those tests, I won't be able to get a refill. And it's just frustrating to me because if you don't take [PrEP] for some time, you're not protected."

A 21-year-old transgender man addressed the significant challenges in navigating referral pathways for PrEP. "I've navigated through referral processes … through mental health, through primary, through PT [physical therapy], through endocrinology, through OBG [obstetrics and gynecology] … it's difficult … because there are so many people on the plan that sometimes, the ball is dropped," he said.

Concern About Side Effects and Interactions with Hormones

Some participants reported experiencing nausea while taking PrEP and needing to take pills with meals. Others,

particularly those who had not used PrEP, mentioned concern about PrEP interacting with their hormone levels. A 20-year-old transgender man shared, "I don't feel the need to take PrEP. But if I did …, I would want to know how PrEP interacts with my hormone levels and my hormone injections." Another participant shared similar concerns regarding side effects with our study team. The 56-year-old transgender man noted, "I think the biggest barrier is the concern about, what is this going to do to you? Will it make my hormones not work? Will it put me at more risk…?".

Experiencing and Anticipating Stigma

Both participants who had and had not used PrEP described stigma as a barrier to PrEP use. For some participants, stigma was a barrier to discussing sexual health and PrEP eligibility with their provider, whereas others were concerned about picking up the medication at the pharmacy or having the pills at home. One respondent suggested disguising the brand so that others would not know it was PrEP.

Regarding their hesitancy to begin PrEP, a 21-year-old transgender man shared, "Stigma, for sure. I would say that is the number one [barrier]. I think maybe putting [PrEP] under a different brand." Another interviewee, a 20-year-old transgender man echoed this sentiment and added, "Family may not be supportive, or their environment may not be safe for them to be taking PrEP or have bottles of that sort of medication in their household."

Outside of social or familial environments, one interviewee added she felt uncomfortable discussing PrEP with her provider. The 42-year-old transgender woman said, "A lot of the times when I go [to the doctor], it doesn't feel like a very affirming or sex-positive environment. So, it's definitely very uncomfortable bringing up those topics in that setting." A separate interviewee addressed additional stigmas transgender women experience in medical settings that may discourage them from accessing PrEP. "I know a lot of transwomen in particular are frustrated with kind of always being associated with HIV," the 56-year-old transgender man stated.

Transgender Participant Suggestions for Improving PrEP Care

Several themes were apparent regarding how PrEP care could be improved. First, participants emphasized the importance of normalizing conversations about sexual health and HIV risk as part of primary care for all individuals regardless of gender identity or sexual orientation, to reduce stigma and discomfort around these topics. They felt that these conversations should be tailored to their gender identities and based on their medical record, using appropriate pronouns, and asking relevant questions. One interviewee, a 42-year-old transgender woman suggested, "Normalize the environment…and that'll go a long way to building trust with a provider, which opens up options for sexual health, mental health, that is affirming and non-shameful." The 20-year-old transgender man added, "I think they should definitely emphasize that PrEP isn't just for gay cis-men."

Second, participants wanted better access to information on PrEP for their gender identity and context, including transparent information on potential side effects, interactions with other medications, effectiveness, and logistics; some participants preferred digital materials and others preferred printed materials for PrEP information. "I'd like to see some testimonials from [PrEP] users. I'd like to know that there is someone like me using it, and they're receiving benefit from it," a 38-year-old transgender woman said. Regarding disseminating information about PrEP, one interviewee, a 31-year-old transgender woman, recommended, "…as far as PrEP, maybe dispelling some common myths, especially within the LGBT and especially in the trans community. I think maybe consistency, reaching out more than once with information about PrEP."

Third, participants wanted fewer appointments and referrals to make taking PrEP easier and more affordable and to minimize chances for negative interactions with new providers. "Making all those steps as streamlined as possible … the fewer people they have to interact with … where there may be a chance for judgement," the 56-year-old transgender man proposed.

Provider Interview Results

Themes that emerged from provider interview data on barriers to PrEP uptake and suggestions for improving PrEP care were consistent to themes identified in the transgender participant interviews.

Providers described the importance of taking sexual histories and assessing HIV/STI risk for new patients. However, they noted that discussing sexual history and behavior can be challenging for both transgender patients and providers depending on their comfort level, and that the use of clinical terms can be seen as insensitive and impede communication.

PCPs also recognized the role of stigma, misgendering, and stereotypes about HIV risk among transgender individuals, corresponding with themes from the participant interviews. Providers suggested having additional training for PCPs regarding inclusive care for transgender and gender diverse patients, as well as training on taking sexual histories and assessing PrEP eligibility.

One provider noted that "…it's still very inadequately trained clinicians that need training to develop a strong comfort with discussing sexual practices" with their patients, while another shared "…there are still a lot of physicians that are really uncomfortable about starting the

conversation about PrEP with transgender patients and making sure they're using the right pronouns and making sure they're asking the right questions." To address these issues, one provider suggested that "[C]onducting an interview with a transgender member is another education piece and an opportunity that we have to educate our colleagues and our physicians. To say, 'Hey, when you encounter a transgender member, this is how you're going to provide care.' And make it very smooth and streamlined and as comfortable as if it were any other member."

Regarding working with trans adolescents, a provider said, "A lot [of pediatric PCPs] were not comfortable becoming aware of [PrEP], which means that their patients who need it would probably not find out about it until after they turned 18. And by that time, they might have already been exposed to HIV."

One provider mentioned that the pandemic-driven shift to virtual care might help some providers and patients to be more comfortable having sensitive conversations. They said, "From a virtual aspect, I see that there's a huge opportunity. [In person] that same patient may very well be uncomfortable talking to their PCP about PrEP. Who, in turn, may also be uncomfortable talking to a transgender [patient] to begin with, let alone about sex, let alone about PrEP that he may or may not know anything about."

Some PCPs indicated that they increasingly conduct their own PrEP assessment and management instead of referring patients to infectious disease providers or HIV primary care providers, although other PCPs continue to refer. Providers suggested that training and supporting more PCPs to manage PrEP prescription and follow-up care might help to improve PrEP uptake, including among transgender individuals. One provider noted, "PrEP management doesn't necessarily need to be done by infectious disease. This can be done by any trained primary care physician. The physician's lack of education is a barrier, on what PrEP is and who is a candidate for it."

However, some providers did not think referral was a barrier to PrEP uptake. Providers recognized routine lab work as an important component of PrEP management, and most providers acknowledged that frequent PrEP follow-up visits and testing can be challenging for patients. "So, the frequency of the testing is probably not the easiest thing for my patients who are working multiple jobs. Like lab hours are always tricky," a provider said. Discussing the barriers regarding follow-up care for their own patients, another provider observed, "My few transgender patients that I have on PrEP are usually very hard to continue [on PrEP] because of lack of follow-up. Missing their appointments, don't get their labs, or simply just falling off the edge of the earth."

Discussion

This mixed-methods study identified multiple patient, provider, and health system-level barriers to PrEP uptake and opportunities to improve PrEP care for transgender and gender diverse individuals in a large U.S. health care system. Our results add to the limited literature on PrEP access and use among transgender and gender diverse individuals in the U.S., drawing from a large, demographically diverse population, compared to other studies that focus on subsets of individuals with known HIV risk factors [4].

Multiple studies have found strikingly low PrEP uptake among transgender individuals [6, 20, 24, 25]. In a nationwide online survey of HIV negative transgender men and women, only 17.4% of individuals in the sample reported ever receiving a PrEP prescription, and PrEP prescriptions were more commonly reported by transgender men than by transgender women [26]. In our study including transgender and gender diverse individuals, most survey respondents had heard of PrEP, but knowledge on how to use PrEP was suboptimal. More than one third of individuals reported some HIV risk factors, but < 5% of had ever taken PrEP.

Results of our study are also consistent with several other studies that have identified knowledge gaps as a barrier to PrEP use among transgender and gender diverse individuals. Despite high general PrEP awareness, limited knowledge and misinformation about PrEP use has been reported [20]. Concern about side effects and drug interactions of PrEP with gender-affirming hormones has also been cited as a primary reason for reluctance to use PrEP, despite evidence that PrEP does not affect levels of hormones [24]. These barriers might be addressed through printed and/or digital information about PrEP, featuring images of transgender and gender diverse individuals and providing PrEP details tailored to these populations.

Even in settings with relatively high access to PrEP, logistical challenges with time and costs required for PrEP-related laboratory tests and care appointments can be barriers to PrEP uptake and reasons for discontinuation [27]. Depending on their individual health plans, KPSC members have a range of co-pays and deductibles. For some individuals, financial barriers to accessing PrEP may include co-pays for visits and laboratory tests, as well as costs of transportation, cost of childcare, or having to take unpaid time off work for appointments. Others may have inadequate information about potential co-pays and have the perception that costs will be prohibitive. Streamlining PrEP care by equipping more PCPs to prescribe PrEP, providing options for virtual visits, regular home HIV testing, and STI self-testing, and reducing the number of in-person provider visits and laboratory tests may help save costs

and time, thereby facilitating PrEP uptake and retention [28, 29]. Such interventions might be particularly helpful for transgender and gender diverse individuals, for whom less in-person visits may be viewed as less opportunity for negative interactions with providers [17]. Furthermore, data have shown that referrals can result in missed opportunities for PrEP care [30]. During the COVID-19 pandemic, KPSC transitioned to providing virtual visits for PrEP, which may help improve PrEP uptake and persistence in the future.

Experience or anticipated stigma from providers and peers is commonly cited as a barrier to PrEP [16, 19, 31]. Consistent with other studies, some transgender participants in our study reported frustration that transgender women are frequently associated with HIV [24]. However, other participants, particularly transgender men, reported that their providers did not discuss HIV risk factors or whether PrEP might be beneficial. Emphasis only on HIV risk in transgender women and cisgender men who have sex with men may inadvertently overlook prevention opportunities among gender diverse or transgender men who may benefit from PrEP. Integrating sexual health and PrEP eligibility assessments into routine care, regardless of gender identity or sexual orientation, may also help reduce stigma. Provider training is needed to increase provider sensitivity and inclusivity to care for transgender and gender diverse individuals, in general, and specifically for PrEP [32, 33].

Previous studies have identified mental health concerns such as depression and anxiety as barriers to PrEP uptake and adherence for transgender women [34, 35]. In our study, more than 30% of survey respondents reported receiving diagnoses of depression and anxiety, while 9% and 4% noted diagnoses of post-traumatic stress disorder (PTSD) and bipolar disorder, respectively. These proportions do not include undiagnosed conditions and thus may underestimate the true burden of mental health conditions among transgender and gender diverse individuals in our study. These findings underscore the importance of routine mental health screenings as part of PrEP care and emphasize the need for a more collaborative PrEP and mental health care model.

Limitations

Our study has several limitations. First, survey results may not be generalizable to the underlying transgender and gender diverse population, as the response rate was low, and based on sociodemographic characteristics, survey respondents may have had fewer HIV risk factors compared to non-respondents. Additionally, survey results may not be generalizable to other health care systems in settings with different local and state policies. Second, because we expected PrEP use to be low in this population, the survey was not designed to measure PrEP persistence, but this is an area for potential further research. Third, survey responses and interviews may have been subject to recall and social desirability biases, but we attempted to mitigate this by taking time to build rapport at the beginning of the interview and using a semi-structured interview guide with probing questions. Fourth, we have few adolescent PrEP users in our health system, therefore we were unable to include adolescents in this study. A strength of this study is the embedded nature within a large learning health care system, which facilitates next steps to develop and implement multipronged interventions to improve PrEP access and care for transgender and gender diverse individuals at KPSC.

Conclusion

This study highlights very low uptake of PrEP among transgender and gender diverse individuals and substantial patient, provider, and health system-level barriers to PrEP uptake and retention in care. Further work is needed to address these barriers and to implement and evaluate interventions to train and support providers, increase PrEP knowledge, and streamline PrEP care.

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Author Contributions KB and RH conceived and designed the study; RH acquired funding; CP, MM, and KP collected the data; CP, MM, and KP analyzed the data; all authors interpreted the data; KB and CP drafted the manuscript; all authors reviewed and approved the manuscript and take responsibility for appropriate portions of the content.

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Data Availability Individual-level data reported in this study are not publicly shared. Upon reasonable request and subject to review, KPSC may provide the de-identified aggregate-level data that support the findings of this study.

Code Availability N/A.

Declarations

Competing Interests Katia Bruxvoort has received funding from Dynavax, GlaxoSmithKline, Moderna, Pfizer, and Seqirus for research unrelated to this study. All other authors have no competing interests.

Ethical Approval The study was approved by the KPSC Institutional Review Board (IRB #12482).

Consent to Participate The requirement for written informed consent was waived by the KPSC IRB due to minimal risk to study participants. Individuals who voluntarily completed the survey provided tacit agreement to participate. Individuals who participated in qualitative interviews provided verbal agreement prior to participation.

Consent for Publication N/A.

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